of paliperidone palmitate on the results of chemistry and hematology laboratory tests (including liver and renal function tests, serum lipid levels, and glucose levels) did not show clinically relevant differences from those of placebo.

Local injection site tolerability was good. Occurrences of induration, redness, or swelling as assessed by blinded study personnel were infrequent, generally mild, decreasing over time, and similar in incidence for the paliperidone palmitate and placebo groups. Investigator ratings of injection pain were similar for the placebo and paliperidone palmitate groups.

Study Limitations:

This study investigated the efficacy and safety of paliperidone palmitate for acute treatment of schizophrenia over 13 weeks and does not provide information on longer term treatment. The study was not designed to detect differences between doses of paliperidone palmitate; thus, dose-related trends in efficacy and safety can only be described descriptively. The study was also not designed to demonstrate efficacy for specific subgroups of subjects, such as those from a particular country. An independent, centralized blinded rating service was used for performing all ratings of PANSS, PSP and CGI-S for all subjects enrolled at U.S. sites. The investigators at these sites did not complete any of the ratings, which would have provided a reference for ratings provided by the rating service. Thus, data from this study cannot be used to fully evaluate the utility of using blinded independent raters for detecting treatment differences.

Conclusion:

All 3 doses of paliperidone palmitate tested in this study—25, 100, and 150 mg eq.—were efficacious in adult subjects with schizophrenia who were experiencing acutely exacerbated schizophrenia. Specifically, the results of the primary efficacy endpoint (change from baseline to end point in PANSS total score) demonstrated statistical superiority of paliperidone palmitate 25 mg eq., 100 mg eq., and 150 mg eq. over placebo. Significantly greater improvement in subjects' personal and social functioning (as measured by the PSP score) was also seen for the paliperidone palmitate 100 mg eq. and 150 mg eq. doses compared with placebo, and global improvement was validated by a favorable and statistically significant CGI-S change for these 2 dose groups. There was a dose response in the primary and secondary efficacy endpoints (PANSS, PSP, and CGI-S). All 3 doses of paliperidone palmitate, including the highest dose of 150 mg eq., were well tolerated, suggesting a positive benefit-risk ratio across the dose range currently studied. No new safety signal was detected.

FIGURES

FIGS. **1-3** graphically presents the observed versus population pharmacokinetics model simulation for plasma paliperidone concentrations. The line indicates the median values calculated from population pharmacokinetic simulation. The shading indicates 90% prediction interval representing the between and within subject, variability obtained using the population pharmacokinetic simulation. The circles indicate observed plasma paliperidone concentrations. The arrows indicate the days when paliperidone palmitate injection was given. As is apparent from the Figures the plasma profiles provided by initiating paliperidone with 150 mg eq. followed by a subsequent dose of 100 or 150 for days 1-36 provide a rapid rise to a therapeutic dose levels. Most preferably the dosing of paliperidone to patients should be maintained within ±25%, preferably 20% of the median plasma concentrations provided in these figures for days 1-36. For patients whose dosing continues at 100 mg eq. the preferably the dosing of paliperidone to patients should be maintained within ±25%, preferably 20% of the median plasma concentrations provided in FIG. **2** for days 1-64. For patients whose dosing continues at 150 mg eq. the preferably the dosing of paliperidone to patients should be maintained within ±25%, preferably 20% of the median plasma concentrations provided in FIG. **3** for days 1-64.

We claim:

1. A dosing regimen for administering paliperidone palmitate to a psychiatric patient in need of treatment for schizophrenia, schizoaffective disorder, or schizophreniform disorder comprising

(1) administering intramuscularly in the deltoid of a patient in need of treatment a first loading dose of about 150 mg-eq. of paliperidone as paliperidone palmitate formulated in a sustained release formulation on the first day of treatment;

(2) administering intramuscularly in the deltoid muscle of the patient in need of treatment a second loading dose of about 100 mg-eq. of paliperidone as paliperidone palmitate formulated in a sustained release formulation on the 6^{th} to about 10th day of treatment; and

(3) administering intramuscularly in the deltoid or gluteal muscle of the patient in need of treatment a first maintenance dose of about 25 mg-eq. to about 150 mg-eq. of paliperidone as paliperidone palmitate in a sustained release formulation a month (±7 days) after the second loading dose.

2. The dosing regimen of claim **1** wherein after administration of the first maintenance dose, subsequent maintenance doses of from about 25 mg-eq. to 150 mg-eq. are administered in the deltoid or gluteal muscle of the psychiatric patient in need of treatment at monthly (±7 days) intervals.

3. The dosing regimen of claim **1** wherein the sustained release formulation is an aqueous nanoparticle suspension.

4. A dosing regimen for administering paliperidone palmitate to a psychiatric patient in need of treatment for psychotic disorder comprising

(a) administering intramuscularly in the deltoid of a patient in need of treatment a first loading dose of about 150 mg-eq. of paliperidone as paliperidone palmitate formulated in a sustained release formulation on the first day of treatment;

(b) administering intramuscularly in the deltoid muscle of the patient in need of treatment a second loading dose of about 100 mg-eq. of paliperidone as paliperidone palmitate formulated in a sustained release formulation on the eighth day of treatment; and

(c) administering intramuscularly in the deltoid or gluteal muscle of the patient in need of treatment a first maintenance dose of about 25 mg-eq. to about 150 mg-eq. of paliperidone as paliperidone palmitate in a sustained release formulation a month (±7 days) after the second loading dose.

5. The dosing regimen of claim **4** wherein the sustained release formulation is an aqueous nanoparticle suspension.

6. The dosing regimen of claim **4** wherein the psychiatric patient is in need of treatment for psychotic disorder wherein the psychotic disorder is schizophrenia.

7. The dosing regimen of claim **4** wherein the psychiatric patient is in need of treatment for a psychotic disorder wherein the psychotic disorder is schizoaffective disorder.

8. A dosing regimen for administering paliperidone palmitate to a renally impaired psychiatric patient in need of